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EXAMINER	
HUYNH, PHUONG N	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/580,108	QASBA ET AL.	
	Examiner	Art Unit	
	PHUONG HUYNH	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 June 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-45* is/are pending in the application.

4a) Of the above claim(s) *4-7 and 13-42* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3, 8-12 and 43-45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *19 May 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/13/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-45 are pending.

2. Applicant's election with traverse of Group I, Claims 1-12 and 43-45 (now claims 1-3, 8-12 and 43-45) drawn to a specific targeted glycoconjugate comprising a specific bioactive agent and a specific targeting compound wherein the bioactive agent and targeting compound are joined by a specific modified saccharide compound that read on the species of polypeptide as the bioactive agents, the glycoprotein as the species of targeting compound and the galactose as the species of modified saccharide compound, filed June 13, 2008, is acknowledged. The traversal is on the grounds that it is believed that multiple groups can be search and examined together without undue burden.

Applicants' traversal has been fully considered but is not deemed persuasive for the same reasons of record in the restriction mailed March 26, 2008.

The inventions listed as Inventions 1-4 do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

A same or corresponding technical feature shared among Inventions 1-4 is a glycoconjugate comprising a bioactive agent and a targeting compound wherein the bioactive agent and targeting compound are joined by a specific modified saccharide compound. However, the US Pat No 5,608,060 (issued March 1997; PTO 892) teaches a targeted glycoconjugate comprising a targeting compound such as avidin/biotin-targeting moiety (e.g. antibody) conjugate (see col. 10, lines 64 through col. 11, col. 18, lines 17-63, in particular), a drug moiety such as therapeutic agent, toxin or radionuclide (see col. 4, line 17-20, col. 13-14, in particular) joined by a modified saccharide compound such as galactosyl-biotinyl-human BSA clearing agent where the galactosyl is derivatized to expose or incorporated galactose residue (see col. 19, line 20-67, in particular).

Thus, the same or corresponding technical feature is not special since it was known in the prior art and therefore cannot make a contribution over the prior art. Since the inventions lack the same or corresponding special technical feature, then the

inventions listed as Inventions 1-4 are not so linked as to form a single general inventive concept under PCT Rule 13.1.

Contrary to applicants' assertion that multiple groups can be search without undue burden, the species of glycoconjugate comprising distinct bioactive agent such as the ones recited in claim 2, the distinct targeting compound such as glycoprotein, glycolipid or carbohydrate, antibody, receptor ligand, via distinct modified saccharide such as galactose, Glucose (Glc), D-deoxy-Glc, arabinose, GalNAc or GlcNAc for treating distinct diseases such as cancer, inflammatory disease, hormone deficiency disease, hormone abnormality due to hypersecretion, infectious diseases such as bacterial infection, viral infection, fungal infection, parasitic infection, cardiovascular disease, genetic disease, autoimmune disease, allergic reaction, organ rejection (graft-versus-host disease), and immune deficiency such as AIDs are independent or distinct because claims to the different species recite the mutually exclusive characteristics. The glycoconjugates have different structure, different target specificity and treating different diseases that differ with respect to their etiology, method steps and endpoints. Therefore, they are patentably distinct.

Therefore, the requirement of Group I and Groups II-IV is still deemed proper and is therefore made FINAL.

3. Claims 4-7 and 13-42 are withdrawn from further consideration by the examiner, 37 C.F.R. 1.142(b) as being drawn to non-elected inventions.

4. Claims 1-3, 8-12 and 43-45, drawn to a specific targeted glycoconjugate comprising a specific bioactive agent and a specific targeting compound wherein the bioactive agent and targeting compound are joined by a specific modified saccharide compound that read on the species of polypeptide as the bioactive agents, the glycoprotein as the species of targeting compound and the galactose as the species of modified saccharide compound, are being acted upon in this Office Action.

5. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-3, 8-12 and 43-45 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling only for a targeted glycoconjugate comprising a specific bioactive agent and a specific targeting compound wherein the bioactive agent and the targeting compound are joined by a modified UDP galactose—Acetyl group (UDP-GalNAc) having a ketone functional group appended at the C-2 position of the galactose ring using the mutant Y289L galactose transferase for detection assays, **does not** reasonably provide enablement for any targeted glyconjugate comprising any bioactive agent and any targeting compound wherein the bioactive agent and the targeting compound are joined by any modified saccharide compound for use in any medical therapy as set forth in claims 1-3, 8-12 and 45, (2) any pharmaceutical composition comprising any targeted glyconjugate comprising any bioactive agent and any targeting compound wherein the bioactive agent and the targeting compound are joined by any modified saccharide compound as set forth in claim 43 and (3) a kit comprising any targeted glyconjugate comprising any bioactive agent and any targeting compound wherein the bioactive agent and the targeting compound are joined by any modified saccharide compound as set forth in claim 44 for use in any therapeutic or diagnostic methods. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in **scope** with these claims.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention. The specification disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without an undue amount of experimentation.

The claims encompass innumerous targeted glyconjugate comprising any bioactive agent and any targeting compound wherein the bioactive agent and the targeting compound are joined by any modified saccharide compound for use in any medical therapy.

Enablement is not commensurate in scope with how to make any targeted glyconjugate comprising any bioactive agent and any targeting compound wherein the bioactive agent and the targeting compound are joined by any modified saccharide compound for treating any diseases or diagnosis.

The specification discloses only labeling of CREB or bovine lens α-crystallin using recombinant O-GlcNAc glycosylated CREB and the mutant Y289L O-GlcNAc glycosyltransferase, see pages 45-46. The specification discloses only modified UDP galactose--Acetyl group (UDP-GalNAc) having a ketone functional group appended at the C-2 position of the galactose ring because the mutant Y289L galactose transferase has been shown to tolerate unnatural substrates containing minor substitution at the C-2 position, including 2-deoxy, 2-amino, and 2-Acetyl substituents, see page 48 of the specification and summary of the specification.

However, the essential or critical features of the claimed limitation modified galactose residue having a ketone group at C2 position of the galactose (see summary of invention, page 25, line 5-6, in particular) and the use of recombinant mutant Y289L galactose transferase to enable near stoichiometric labeling or conjugation which applicant describes as an essential or critical feature of the invention are not recited in the claims. A claim which omits matter disclosed to be essential to the invention as described in the specification or in other statements of record may also be subject to rejection under 35 U.S.C. 112, para. 1, as not enabling, or under 35 U.S.C. 112, para. 2. See *In re Mayhew*, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976); *In re Venezia*, 530 F.2d 956, 189 USPQ 149 (CCPA 1976); and *In re Collier*, 397 F.2d 1003, 158 USPQ 266 (CCPA 1968). See also MPEP § 2172.01.

Further, enablement is not commensurate in scope with how to use any targeted glyconjugate comprising any bioactive agent and any targeting compound wherein the bioactive agent and the targeting compound are joined by any modified saccharide compound for treating any diseases or diagnosis.

The specification provided little or no guidance as to the binding specificity of the targeting compound beyond the mere mentioned of a laundry list of targeting molecules, bioactive agents joined by a list of modified saccharide compounds. The specification merely asserts that the claimed treat numerous diseases including AIDS, see page 30 of specification. There is no guidance as to the binding specificity of the targeting compound in the claimed

glycoconjugates. Given the numerous glycoconjugates, there is a lack of *in vivo* working example of such glycoconjugate could treat any diseases such as AIDS.

Pharmaceutical composition in the absence of *in vivo* data are unpredictable for the following reasons: (1) the protein may be inactivated before producing an effect, i.e. such as proteolytic degradation, immunological inactivation or due to an inherently short half-life of the protein; (2) the protein may not reach the target area because, i.e. the protein may not be able to cross the mucosa or the protein may be adsorbed by fluids, cells and tissues where the protein has no effect; and (3) other functional properties, known or unknown, may make the protein unsuitable for *in vivo* therapeutic use, i.e. such as adverse side effects prohibitive to the use of such treatment. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992).

The specification does not adequately teach how to effectively treat any diseases or diagnosing any diseases using any targeted glyconjugate comprising any bioactive agent and any targeting compound wherein the bioactive agent and the targeting compound are joined by any modified saccharide without guidance as to the binding specificity of such glycoconjugate to the development of effective in vivo human therapeutic compositions, commensurate in scope with the claimed invention. Therefore, it is not clear that the skilled artisan could predict the efficacy of the conjugate exemplified in the specification or the breadth of glycoconjugate for treating any diseases, encompassed by the claims.

For these reasons, it would require undue experimentation of one skilled in the art to practice the claimed invention. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992).

In re wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988), the decision of the court indicates that the more unpredictable the area is, the more specific enablement is necessary. In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims, it would take an undue amount of experimentation for one skilled in the art to practice the claimed invention.

8. Claims 1-3, 8-12 and 43-45 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

Claims 1 and 45 are broadly drawn to any targeted glyconjugate comprising any bioactive agent and any targeting compound wherein the bioactive agent and the targeting compound are joined by any modified saccharide compound for use in any medical therapy.

Claim 2 is broadly drawn to any targeted glyconjugate comprising any bioactive agent such as any polypeptide and any targeting compound wherein the bioactive agent and the targeting compound are joined by any modified saccharide compound.

Claim 3 is broadly drawn to any targeted glyconjugate comprising any bioactive agent and any targeting compound such as any glycoprotein wherein the bioactive agent and the targeting compound are joined by any modified saccharide compound.

Claim 8 is broadly drawn to any targeted glyconjugate comprising any bioactive agent and any targeting compound wherein the bioactive agent and the targeting compound are joined by any modified saccharide compound such as modified galactose.

Claim 9 is broadly drawn to any targeted glyconjugate comprising any bioactive agent and any targeting compound wherein the bioactive agent and the targeting compound are joined by any modified galactose further comprises any reactive functional group.

Claim 10 is broadly drawn to any targeted glyconjugate comprising any bioactive agent and any targeting compound wherein the bioactive agent and the targeting compound are joined by any modified galactose further comprises any reactive functional group such as ketone group.

Claim 11 is broadly drawn to any targeted glyconjugate comprising any bioactive agent and any targeting compound wherein the bioactive agent and the targeting compound are joined by any modified galactose further comprises any reactive functional group attached to the C2 position of the saccharide ring.

Claim 12 is broadly drawn to any targeted glyconjugate comprising any bioactive agent and any targeting compound wherein the bioactive agent and the targeting compound are joined by any modified galactose further comprises any reactive functional group attached to the C2 position of the galactose ring.

Claim 43 is broadly drawn to a pharmaceutical composition comprising any targeted glyconjugate comprising any bioactive agent and any targeting compound wherein the bioactive agent and the targeting compound are joined by any modified saccharide compound and a pharmaceutically acceptable carrier.

Claim 44 is broadly drawn to a kit comprising any targeted glyconjugate comprising any bioactive agent and any targeting compound wherein the bioactive agent and the targeting compound are joined by any modified saccharide compound and instruction for use in any therapeutic or any diagnostic methods.

The scope of the each genus includes many members with widely differing structural, chemical, and physiochemical properties such as widely differing amino acid sequences, nucleotide sequences, and biological functions. Furthermore, each genus is highly variable because a significant number of structural and biological differences between genus members exist.

For claims drawn to a genus, MPEP § 2163 states the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show that applicant was in possession of the claimed genus. See *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483. In *Fiddes v. Baird*, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provides only the bovine sequence.

In this case, the specification does not reasonably provide a **written description** for any targeted glyconjugate comprising any bioactive agent and any targeting compound wherein the

bioactive agent and the targeting compound are joined by any modified saccharide compound for use in any medical therapy.

At the time of filing, the specification discloses only labeling of CREB or bovine lens α-crystallin using recombinant O-GlcNAc glycosylated CREB and the mutant Y289L O-GlcNAc glycosyltransferase, see pages 45-46. The specification discloses only modified UDP galactose--Acetyl group (UDP-GalNAc) having a ketone functional group appended at the C-2 position of the galactose ring because the mutant Y289L galactose transferase has been shown to tolerate unnatural substrates containing minor substitution at the C-2 position, including 2-deoxy, 2-amino, and 2-Acetyl substituents, see page 48 of the specification and summary of the specification.

At the time of filing, applicants are not in possession of a genus of targeted glyconjugate comprising any bioactive agent and any targeting compound wherein the bioactive agent and the targeting compound are joined by any modified saccharide compound for use in any medical therapy or any diagnostic method. The specification provided little or no guidance as to the binding specificity of the targeting compound beyond the mere mentioned of a laundry list of targeting molecules, bioactive agents joined by a list of modified saccharide compounds. The specification merely asserts that the claimed treat numerous diseases including AIDS, see page 30 of specification. There is no guidance as to the binding specificity of the targeting compound in the claimed glycoconjugates. There is no disclosure of any *in vivo* working example that the claimed glyconjugate could treat any disease such as AIDS, cancer, any autoimmune diseases, any bacterial infections, any psychiatric diseases, any cardiovascular diseases, etc. In this case, the specification fails to disclose a representative number of species of each claimed genus, which includes many members with widely differing structural, chemical, and biological functions. MPEP § 2163 states that a representative number of species means that the species which are adequately described are representative of the entire genus.

Further, the essential or critical features of the claimed limitation modified galactose residue having a ketone group at C2 position of the galactose (see summary of invention, page 25, line 5-6, in particular) and the use of recombinant mutant Y289L galactose transferase to enable near stoichiometric labeling or conjugation which applicant describes as an essential or critical feature of the invention are not recited in the claims and does not comply with the written description requirement. See *Gentry Gallery*, 134 F.3d at 1480, 45 USPQ2d at 1503; *In re Sus*, 306 F.2d 494, 504, 134 USPQ 301, 309 (CCPA 1962) ("[O]ne skilled in this art would not be

taught by the written description of the invention in the specification that any 'aryl or substituted aryl radical' would be suitable for the purposes of the invention but rather that only certain aryl radicals and certain specifically substituted aryl radicals [i.e., aryl azides] would be suitable for such purposes.") (emphasis in original). Compare *In re Peters*, 723 F.2d 891, 221 USPQ 952 (Fed. Cir. 1983) (In a reissue application, a claim to a display device was broadened by removing the limitations directed to the specific tapered shape of the tips without violating the written description requirement. The shape limitation was considered to be unnecessary since the specification, as filed, did not describe the tapered shape as essential or critical to the operation or patentability of the claim.).

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.).

With the exception of the specific modified galactose residue having a ketone group at C2 position of the galactose linked to a specific targeting agent and a specific bioactive agent using the specific recombinant mutant Y289L galactose transferase for detection assays, the skilled artisan cannot envision the detailed chemical structure of the encompassed glycoconjugate and binding specificity of the targeting compound for treating or diagnosing any diseases. Therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993)and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

Because the described labeling of CREB or bovine lens α-crystallin using modified galactose residue having a ketone group at C2 position of the galactose linked to a specific targeting agent and a specific bioactive agent using the specific recombinant mutant Y289L galactose transferase for detection assays is not representative of the entire claimed genus, and the specification does not disclose structural features shared by members of the genus, one of skill in the art would conclude that applicant was not in procession of the claimed genus because

Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. § 112 is severable from its enablement provision (see page 1115).

Applicant is directed to the Final Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001and revision of the Written Description Training materials, posed April 11, 2008 http://www.USPTO.gov/web/menu/written.pdf.

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 1-3, 8, and 43-45 are rejected under 35 U.S.C. 102(b) as being anticipated by US Pat No. 5,608,060 (of record, issued March 4, 1997; PTO 892).

The '060 patent teaches various targeted glycoconjugates comprising a targeting moiety such as ligand that binds to EGF receptor, which is a glycoprotein containing galactose residues that direct liver uptake (See col. 3, lines 46-55, col. 4, lines 1-6, col. 22, line 54-57, col. 59, line 54-55, in particular), and bioactive compound such as drugs, radionuclides, anti-tumor agents, or toxin (see col. 4, line 17-20, col. 6, lines 16, col. 13,lines 13-56, in particular) joined by a modified saccharide such as galactose derivatized with 1-5 biotin residues or galactosyl-biotinyl-BSA (see col. 19, lines 20-67, in particular). The '060 patent further teaches a kit comprising the reference targeted glycoconjugates for treating cancer or imaging (see coo. 108, line 39-40, in particular). The '060 patent also teaches a pharmaceutical composition comprising the reference glycoconjugate and a pharmaceutical acceptable carrier such as PBS (see col. 106, lines 6, in particular). Thus, the reference teachings anticipate the claimed invention.

11. Claims 1-3, 8-10, and 43-45 are rejected under 35 U.S.C. 102(e) as being anticipated by US Pat No. 7,265,085 (issued Sept 4, 2007; claimed priority to earliest provisional application 60/328,523 filed Oct 10, 2001; PTO 892).

The '085 patent teaches various targeted glycoproteins such as transferrin-SA linker-GDNF wherein the reference targeting compound such as transferrin and bioactive agent such as

GDNF are joined by a modified saccharide compound such as O-linked SA modified galactose using galactosyl transferase (see col. 349-350, claims 1-4 of '085 patent, back ground of invention, in particular). The reference modified saccharide is galactose or Gal (see summer of invention, paragraph 68, in particular). The modified saccharide or modified sugar such as glycosyl residues have also been modified to contain ketone groups (see paragraph 26, Background of invention, paragraphs 579-592, in particular). The reference modified or oxidized galactose may further comprise a terminal galactose residue to the corresponding aldehyde, see paragraph 25, in Back ground of invention, in particular). The '085 patent also teaches a pharmaceutical composition comprising the reference glycoconjugate and a pharmaceutical acceptable carrier such as PBS or saline (see paragraphs 1189-1193, in particular). The '085 patent also teaches a kit comprising the reference glycoconjugate and instructions for how to use such glycoconjugate (see paragraph 1450, in particular). Thus, the reference teachings anticipate the claimed invention.

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 103(a) that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. This application currently names joint inventors. In considering Patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

14. Claims 1 and 8-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Pat No. 7,265,085 (issued Sept 4, 2007; claimed priority to earliest provisional application 60/328,523 filed Oct 10, 2001; PTO 892) in view of Hang et al (J Am Chem 123: 1242-1243, 2001; PTO 1449) and Nauman et al (Biochimica et Biophysica Acta 1568: 147-154, 2001; PTO 892).

The teachings of the '085 patent have been discussed supra. The '085 patent further teaches glycopeptide molecule having a modified sugar molecule or other compound conjugated thereto confers a beneficial property on the peptide; the conjugate molecule is added to the peptide enzymatically because enzyme-based addition of conjugate molecules to peptides has the advantage of regioselectivity, stereoselectivity and having desired and or modified glycan structures that can be produce at an industrial scale for the efficient production of improved therapeutic peptides (see summary of invention).

The invention in claim 11 differs from the teachings of the reference only in that the glycoconjugate wherein the reactive functional group is attached to the C2 position of the saccharide ring instead of any position in the saccharide ring.

The invention in claim 12 differs from the teachings of the reference only in that the glycoconjugate wherein the reactive functional group is attached to the C2 position of the galactose ring instead of any position in the galactose ring.

Hang et al teach the use of unnatural or modified monosaccharide such as 2-ketosugars or 2-keto isostere of GalNAc (galacto-N-Acetyl) sugar or 2-N-acetaminodugars as the substrate for GalNAc transferase for metabolic glycoprotein engineering in CHO cells; the 2-Keto GalNAc might be exploited to introduce unique chemical reactivity into secreted glycoproteins produced by large-scale recombinant expression, allowing further selective modification (see page 1243, col. 2, last paragraph, in particular). Hang et al further teach the ketone reactive group produced by 2-ketosugars can be used as a molecular handle and more accessible for chemical reaction with biotin hydrazide (see page 1243, col. 1-2, in particular).

Nauman et al teach condensation of aldehydes or ketones with hydrazines or aminooxy compounds is an example of highly selective covalent reaction (see page 147, col. 2, in particular). Nauman et al teach the ketone group can be incorporated into cell surface oligosaccharides by metabolic engineering. The ketone bearing modified sugar such as N-acetyl mannosamine can react with a number of nucleopiles such as hydrazide or aminooxy compounds that allow the ligation or conjugation of any external delivered ligands such as drug for tumor cell targeting (see page 148, paragraph bridging col. 1 and 2, page 149, col. 1, in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the linker substrate of O-linked SA modified galactose of the '085 patent for the 2-ketosugars or 2-keto isostere of GalNAc as taught by Hang et al for producing targeted glycoconjugate comprising bioactive agent GDNF and a targeting compound

transferrin joined by the modified 2-Keto GalNAc at the C2 position of galactose as taught by the '085 patent and Hang et al.

One having ordinary skill in the art would have been motivated to do use 2-ketosugars or 2-keto isostere of GalNAc (galacto-N-Acetyl) sugar or 2-N-acetaminodugars as the substrate for conjugation because Hang et al teach the 2-Keto GalNAc might be exploited to introduce unique chemical reactivity into secreted glycoproteins produced by large-scale recombinant expression, allowing further selective modification (see page 1243, col. 2, last paragraph, in particular). One having ordinary skill in the art would have been motivated to do use 2-ketosugars or 2-keto isostere of GalNAc (galacto-N-Acetyl) sugar or 2-N-acetaminodugars as the substrate for conjugation because Hang et al teach the ketone group can be used as a molecular handle and more accessible for chemical reaction with biotin hydrazide (see page 1243, col. 1-2, in particular).

One having ordinary skill in the art would have been motivated with the expectation of success to do use 2-ketosugars or 2-keto isostere of GalNAc (galacto-N-Acetyl) sugar or 2-N-acetaminodugars as the substrate for conjugation because the ketone bearing modified sugar can react with a number of nucleopiles such as hydrazide or aminooxy compounds that allow the ligation or conjugation of any external delivered ligands such as drug for tumor cell targeting as taught by Nauman et al (see page 148, paragraph bridging col. 1 and 2, page 149, col. 1, in particular).

One having ordinary skill in the art would have been motivated with the expectation of success to make and use targeted glycoconjugate for drug delivery because the conjugated molecule confers a beneficial property on the peptide by improving the therapeutic index of the drug by reducing non-specific drug toxicity or systemic exposure and targeting concentrate the drug within the site of interest such as tumor as taught by Nauman et al (see page 147, col. 1, in particular).

One having ordinary skill in the art would have been motivated with the expectation of success to make and use targeted glycoconjugate for drug delivery because the '085 patent teaches enzyme-based addition of conjugate molecules to peptides has the advantage of regioselectivity, stereoselectivity and can be produce at an industrial scale for the efficient production of improved therapeutic peptides (see summary of invention). From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

15. No claim is allowed.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phuong Huynh, Ph.D. whose telephone number is (571) 272-0846. The examiner can normally be reached Monday through Thursday from 9:00 a.m. to 6:30 p.m. and alternate Friday from 9: 00 a.m. to 5:30 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Eileen B O'Hara can be reached on (571) 272-0878. The IFW official Fax number is (571) 273-8300.

17. Any information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Phuong Huynh/
Primary Examiner, Art Unit 1644
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